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A CASE OF PERMANENT CONJUGATE DEVIATION OF THE EYES AND HEAD, THE RESULT OF A LESION LIMITED TO THE SIXTH NUCLEUS; WITH REMARKS ON ASSOCIATED LATERAL MOVEMENTS OF THE EYEBALLS, AND ROTATION OF THE HEAD AND NECK.

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THE following case is one of great interest, and of extreme rarity. The patient during life suffered from *permanent* conjugate deviation of the eyeballs and head. This was diagnosed before death to be the result of a lesion of the sixth nucleus on one side. On post-mortem examination a minute softening was found occupying, and limited to, that centre.

Elizabeth G., aged sixty-seven, a domestic servant, was admitted into the Paddington Infirmary on October 11th, 1887. Her family history was unimportant. The patient had always enjoyed good health till the present illness. In August, 1887, having gone to bed one evening in her usual condition, she awoke next morning to find that she was afflicted with complete paralysis of the left upper extremity, otherwise she was quite well. This condition remained unchanged for two months, when one morning on waking, she found in addition, that both her eyes were turned towards the right side, so that she could see nothing in front of her, and that her head was fixedly rotated towards the right side. Three days afterwards she came into the Infirmary. On October 13th her condition was briefly as follows. The patient was weak and confined to bed. Her intelligence appeared normal, and she replied to all questions with accuracy. There was very trifling paresis of the left side of the face. The left upper extremity was motionless throughout, from the shoulder downwards. There was no muscular wasting, and the sensibility of the skin was everywhere intact. The reaction of the tendons and muscles to percussion was comparatively increased in the left

arm. Both eyeballs were firmly and permanently fixed towards the right side, and the strongest efforts of the will could barely bring them towards the middle line, and in this the left eye was specially deficient. When each eye was tested separately the right could be moved to, and even a little beyond, the middle line, but the left did not reach that point. Both eyeballs converged when an object was brought close to them. The pupils were equal and normal. The head was firmly and permanently rotated towards the right, and could not voluntarily be brought into a straight position. The chin was tilted forwards and upwards, due to contraction of the left sterno-mastoid muscle. Both lower extremities, although weak, were equal and apparently not paralysed. The knee-jerk on the left side was somewhat more lively than on the other, but was not materially increased. The special senses were practically normal, although both hearing (especially in the left ear) and vision appeared to be somewhat impaired. Ophthalmoscopic examination showed the media to be slightly opaque, and the fundi healthy. There was no hemiopia. The general functions and organs of the body were normal. From this date till the death of the patient, about a month later (November 14th), the condition remained unchanged. She gradually became weaker, and died comatose, exhibiting all the symptoms above described.

Post-mortem Examination.—With the exception of the nervous system the organs of the body were essentially healthy. *Nervous System.*—The brain weighed forty-six ounces. The dura was thickened and slightly adherent to the cranium. There was a large quantity of sub-arachnoid effusion, and over the surface of the brain a considerable amount of venous congestion. The sinuses were normal. The arteries at the base were thickened and atheromatous. The convolutions of the brain were of normal appearance except the right ascending frontal. This, throughout its whole extent, to within about an inch of the longitudinal fissure was pale flattened, and quite soft to the touch. At the upper part of this convolution, and close to the marginal gyrus was a recent superficial meningeal hæmorrhage about the size of a sixpence. On making a transverse vertical section through the ascending frontal convolution, the softening was seen to be of triangular shape, the base occupying the area above described on the surface, and the apex touching the summit of the internal capsule. This was about three-quarters of an inch in thickness. A secondary descending process could be followed downwards through the right internal capsule and crus cerebri. The brain was otherwise

healthy. On removing the pons and medulla, and making a transverse section exactly at their junction, a small flat circular patch of softening, about the size of a large mustard seed, or more accurately about one-tenth of an inch in diameter, was seen occupying the position of the left sixth nucleus, and limited to it without apparently involving the neighbouring structures, such as the facial fibres (Fig. 1). Otherwise, to the naked eye the

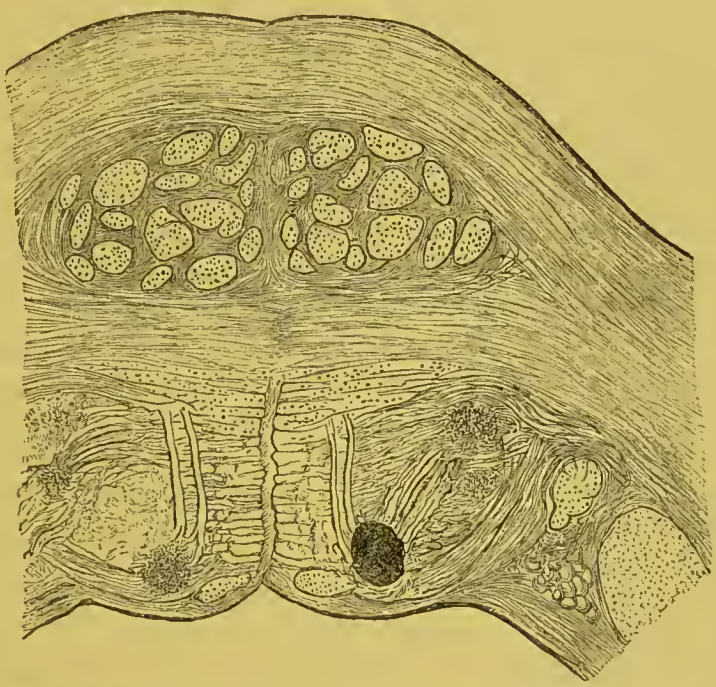

FIG. 1.—Transverse section of the pons at the level of the sixth nucleus showing a limited softening of that centre on the left side (in the woodcut the reverse of the section is seen).

appearances of the pons and medulla were normal. These, with the cord and other nervous structures, were reserved for subsequent and more complete examination, but unfortunately owing to a mishap they were destroyed. The above-described softening in the pons was, however, carefully observed at the post-mortem examination, and an accurate drawing made of it at the time, which is here reproduced. The only structures which were not lost were the two sixth nerves. These were examined with the greatest care, and several independent observers in addition to ourselves—including Drs. Hebb (who kindly made the sections) and Byrom Bramwell—agreed as to the microscopical appearances they exhibited. The right nerve was perfectly healthy. The left here and there showed very slight traces of degenerative atrophy.

Commentary.—The first phase of this patient's condition was paralysis of the left upper extremity. Having been previously in good health, she suddenly during the night lost all power in the entire arm from the shoulder downwards. The muscles were all equally affected; there was no wasting or loss of sensibility, and some weeks afterwards the tendon reflexes were exaggerated. This was associated with very slight paresis of the left side of the face, but the left leg was not perceptibly affected. At no time were any convulsions observed; the intelligence was not seriously impaired and the other organs and functions of the body were normal. This condition remained unchanged until death, three months after the original onset of the symptoms. The diagnosis made during life was that the pyramidal tract between the cortex of the ascending frontal and parietal convolutions, and the upper part of the internal capsule on the right side, was interrupted, slightly encroaching on the facial area. The post-mortem examination showed this surmise to have been substantially correct, and not only were the fibres of the corona radiata underlying these convolutions softened, but almost the entire cortex of the ascending frontal convolution was itself in a similar condition, So far the clinical symptoms perfectly harmonised with what modern experience would lead us to expect from the anatomical distribution of the disease, and therefore call for no further remarks.

The second phase of this case is equally definite, but being much more uncommon, merits careful consideration, as it serves to demonstrate certain very interesting and important physiological facts. About a month before the patient died, having been in her usual condition, she awoke one morning to find that both her eyeballs, as well as her head and neck, were rigidly directed towards the right side, and that no voluntary effort on her part permitted her to bring them, especially the left eye, beyond the middle line. There was marked stiffness and contraction of the left sterno-mastoid muscle. The two eyes in conjunction could not be made to move towards the left, but the right eye was capable of performing a lateral movement towards the left in the act of convergence with both eyes fixed on a near object, or when tested by itself with the left eye closed. In short, there was complete conjugate paralysis of the eyeballs on the left side, the deviation of these towards the right being due to the unopposed action of the healthy muscles on that side, while convergent action of both eyes remained intact. The left

external rectus muscle was completely and permanently paralysed for all purposes. The right internal rectus was only paralysed during the act of conjugation, and contracted normally under all other circumstances. With the exception of the conditions described the patient was otherwise well, and *these symptoms in no way improved, but remained permanently unchanged till her death a month afterwards.*

It is interesting to note that the diagnosis which was hazarded during life was afterwards proved by post-mortem examination to have been correct, namely, that the ocular phenomena were due to a lesion of the left sixth nucleus. It was clear that the conjugate deviation was not the result of fresh extension of the disease in the right cerebral hemisphere, otherwise it would have been of a temporary character and not so complete and permanent as it was in this instance. Any doubt which may have existed during life as to whether the deformity was of a spasmodic or paralytic nature was definitely settled by the post-mortem examination in favour of the latter. The symptoms in no way improving suggested either, interruption of the commissural fibres between the third and sixth nuclei, combined with a second lesion in the motor tract above the latter, or disease of the sixth nucleus itself: the second hypothesis being much the more probable of the two. That a lesion should be so small and so strictly limited to so minute a centre as to annihilate its functions without complicating the neighbouring structures, and notably the facial fibres, is as remarkable as it must be rare, and the result will constitute an important fact in favour of those who, like Duval, Laborde, Graux and Landouzy, have maintained that the sixth nucleus is the reflex centre presiding over that complicated automatism by which the eyeballs, head and neck move harmoniously in concert.

By conjugate movements of the eyeballs is understood that action by which, under an appropriate stimulus, the two eyes move together in turning towards the right or left. This may be a purely reflex or automatic act, or it may be the result of a voluntary impulse, the former being carried on through the agency of a complicated mechanism in the pons, the latter, of course, originating in certain portions of

the cortex cerebri. When both eyeballs look in the same direction, it is due to the contraction of appropriate muscles, and as the external and internal recti are anatomically supplied by different nerves, it is obvious that for conjugate action there must be some association between the sources of this different nervous supply, in order to account for the concerted action. The details of the mechanism by which this is effected may be shortly summarised. The internal recti muscles are supplied by the third, and the external recti by the sixth pair of nerves, each originating from their respective nuclei. When the two eyes look in one direction there is, of course, contraction of the external rectus of one eye, and the internal rectus of the other, which is effected by the action of their corresponding nuclei, namely, the sixth on one side and the third on the other. The simultaneous functionating of these two anatomically distinct centres shows that there is a physiological connection between the two.

The manner in which this is effected is as follows: a sensory stimulus, such as a sudden flash of light, or a loud sound on one side, will reflexly cause both eyes to turn in that direction. This sensory impression is received first by the eye or ear nearest the light or sound, so that through the optic or acoustic nerves on that side it is conveyed to the corresponding sixth nucleus, exciting there a motor impulse which is directly carried by the sixth nerve to the external rectus, thus causing the contraction of that muscle. This eye takes the lead in the action and moves outwards. Almost simultaneously the motor impulse is directed by a crossed communicating track to the third nucleus of the opposite side, and through this by fibres in the third nerve to the corresponding internal rectus muscle, which also contracts. Thus both eyeballs are directed towards the light or sound, the sixth nucleus being the reflex centre by which the combined act is carried on. The afferent impulse is derived from the optic or auditory nerves, and the efferent tracts are, first, the sixth nerve on the same side, and secondly, the crossed fibres joining the sixth nucleus to the third nucleus of the opposite side, as well as some of the fibres continued from thence into the third nerve.

The accompanying diagram (Fig. 2) attempts schematically to show the mechanism by which this process is effected. The different afferent tracts (auditory, *i*; visual, *h*; voluntary, *c*) reach the sixth nucleus (VI.). From thence extend the efferent tracts (*e*) to the external rectus of the same eye, and (*f*, *g*) by the third nucleus (III.) to the internal rectus of the other. The arrangement has been compared to the reins used in driving a pair of horses. When one (*c* for example) is pulled, owing to its bifurcation (*e* and *f g* at VI.) both the animals' heads (the eyeballs?) are drawn in one direction. Some physiologists believe that in addition to the mechanism just described, there is another special centre which intervenes between the retinal and auditory nuclei and the sixth nucleus, and this they place in the superior olivary body. It does not appear that such an assumption is necessary, as the more simple arrangement just described answers all physiological requirements.

That some such disposition as the foregoing must exist is proved by anatomical, physiological and clinical experience. Graux[1] has in the cat actually demonstrated connecting fibres between the third and sixth nuclei. By experiments on dogs the same observer has shown that when the sixth nucleus is artificially destroyed, conjugate paralysis of the eyeballs on the same side, with deviation in an opposite direction, is the result. Finally, clinical facts, and notably the case under consideration, indicate that the same conclusion can be drawn from disease of this ganglion in man.

Thus the mechanism of reflex conjugate movements of the eyeballs may be said to be organised in the pons, and the special centre through which it is carried on is the ganglion to which the name of sixth nucleus has been given by anatomists. Irritation of that group of cells causes conjugate spasm towards the same side, and its destruction produces conjugate paralysis in the same situation, with deviation of the eyeballs in the other direction, the result of the unopposed action of the healthy muscles.

An interesting feature connected with conjugate action

[1] Graux (Gaston), De la Paralysie du Moteur oculaire externe, avec Deviation conjugée. Paris, 1878.

is exemplified by this case, namely the fact that although the muscles connected with this associated phenomenon

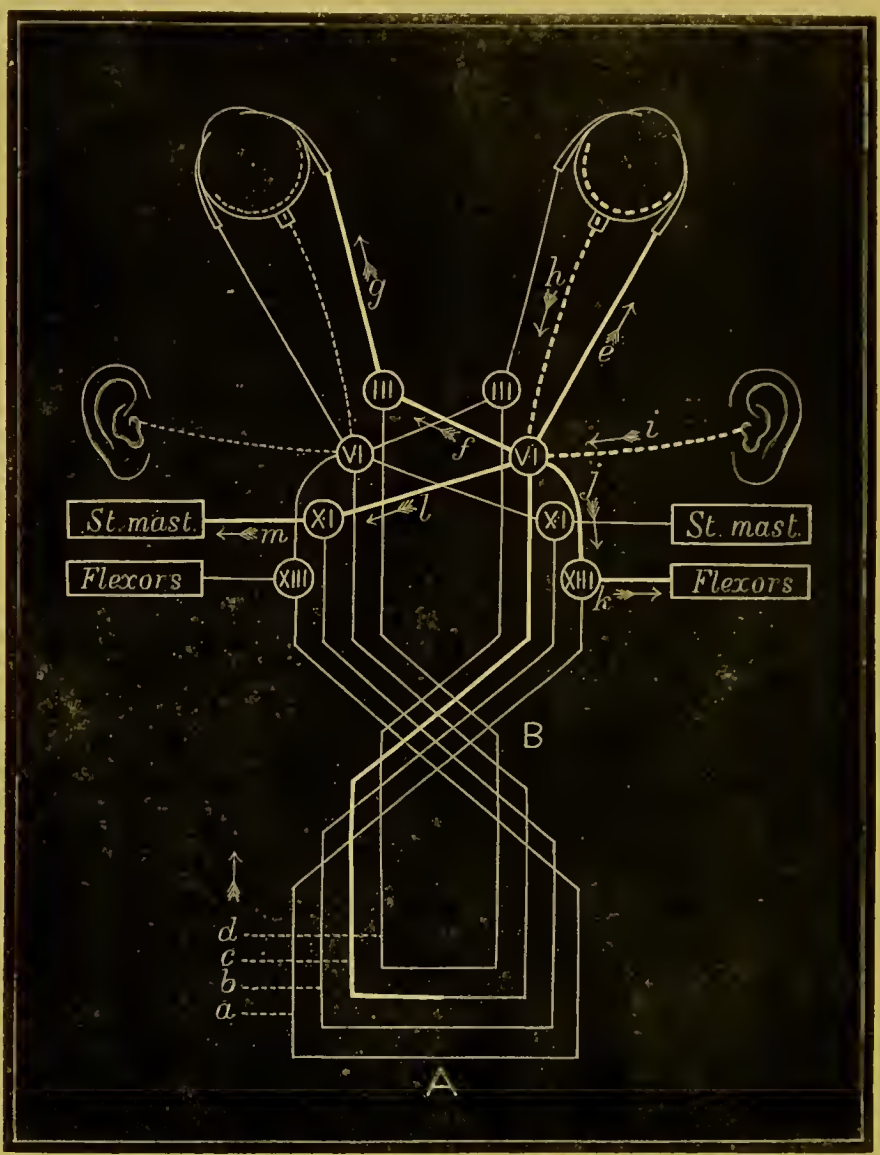

FIG. 2.—*Diagram showing mechanism of conjugate movements of the eyeballs and rotation of the head and neck.*

The thick white lines represent the voluntary motor tract from the cortex to the sixth nucleus, as well as the other efferent tracts from this centre by which conjugate movements of the eyeballs, head and neck are accomplished. The dotted lines indicate the afferent tracts from the eye and ear to the sixth nucleus. The arrows show the direction of the different nerve currents.

A. Cortex Cerebri; *a.* Voluntary tract from cortex to cervical ganglia; *b.* Ditto to eleventh nucleus; *c.* Ditto to sixth nucleus; *d.* Ditto to third nucleus; B. Decussation of voluntary motor tracts in pons and medulla; III. Third nucleus; VI. Sixth nucleus; XI. Eleventh nucleus; XIII. Upper cervical ganglia; *e.* Motor fibres from sixth nucleus to external rectus; *f.* Crossed tract between third and sixth nuclei; *g.* Motor fibres from third nucleus to internal rectus; *h.* Afferent tract from retina to sixth nucleus; *i.* Afferent tract from ear to sixth nucleus; *j.* Communicating tract between sixth nucleus and cervical ganglia on the same side; *k*, Motor nerve from cervical ganglia to flexors of neck; *l.* Crossed tract between sixth and eleventh nuclei of opposite sides; *m.* Motor nerve from eleventh nucleus to sterno-mastoid muscle.

may be paralysed, it does not follow that they lose their function for other purposes. Here for example the internal rectus of one eye was inactive to either the voluntary or reflex impulse of conjugate movement, yet it acted normally when the other eye was closed, and to convergent requirements. In short, this muscle was only cut off from the motor impulses derived from the sixth nucleus, while those connecting it with the third nucleus remained intact (Fig. 2). Therefore all the movements of the right eye were normal except during the act of conjugation, when the internal rectus was immovable. The external rectus of the left eye, on the other hand, was completely and permanently paralysed for all purposes, whether voluntary or reflex, for reasons which the preceding argument must have made obvious.

Although conjugate movements may be of purely reflex production, the same physiological condition may be accomplished as a voluntary act. Impulses from the cortex in connection with the pontine centres are capable of causing the eyeballs to move to the right or left at will. The posterior portion of the frontal convolutions are believed by Ferrier to be the area in which these originate, and both experiment and clinical observation seem to indicate this as the most probable region. Grasset and others believe the angular gyrus and its neighbourhood to be the seat of this process. Whatever the exact area may be, there can be little doubt that conjugate movements of the eyeballs have a definite localisation in the cerebral cortex, as is abundantly shown by experimental and clinical observation. This cortical centre is connected with the

nuclei in the pons by fibres which decussate immediately above them, and the point at which this crossing takes place is believed to be at the corpora quadrigemina. By this means voluntary impulse can be transmitted, and the eyes and head moved conjugately in any direction that may be desired (Fig. 2. *c*). Irritation of the cortex of the brain artificially or by disease causes conjugate spasm. This has been produced in animals, and is frequently seen as one of the initial transitory symptoms of an epileptic or apopletic seizure. Destructive lesions, again, cause conjugate paralysis, which has also been produced experimentally, and is frequently met with clinically, usually in association with severe cases of hemiplegia.

The foregoing phenomena, whether reflex or voluntary, are further rendered more complex by the circumstance, that on the application of an appropriate stimulus, in addition to the eyes, the head and neck also may act conjugately and be directed towards that side, the head being so rotated and inclined as to look over the shoulder.

This conjugate movement of the head with the eyeballs is carried on after the same manner and through the same centres as have just been enumerated, only there is superadded a still more complex series of connections. To the mechanism already formulated, there must be further associations with the sixth nucleus, as the primary starting-point of the special function. Commissural fibres must connect it with the centres for both the rotators and flexors of the head and neck. Movement of the head to one side is effected partly by rotation, and partly by inclination or flexion. The muscles which chiefly come into play for the first purpose, are the sterno-mastoid and trapezius of the opposite side, which are supplied by the spinal accessory nerve, and for the second action the superior oblique, splenius, recti and possibly other muscles on the same side, supplied by cervical nerves, the combined action of which rotates and inclines the head over the shoulder. The diagram (Fig. 2) attempts to show how these various connections may take place, and the relations that may exist between the sixth and eleventh nuclei of opposite sides, and between

the former and the cervical ganglia on the same side. An impulse, whether voluntary (*c*), or from sensory impressions, (*h* and *i*) acting on the sixth nucleus (VI.), through its influence will cause contraction of the external rectus (*e*) and the flexors of the neck (*k*) through connections with the cervical ganglia (XIII.) on the same side; and simultaneously contraction of the internal rectus (*g*), and the sterno-mastoid (*m*) through the eleventh nucleus (XI.) of the opposite side. The result of this is a conjugate movement of both eyeballs, and an inclination and rotation of the head towards the side of the sixth nucleus which receives and distributes the impulse. Destruction of this centre would of course have exactly the opposite effects.

Such then is an attempt to explain the mechanism of the highly complex physiological phenomenon, conjugate movement of the eyeballs and head—an act which partly by inheritance and partly by education, has become organised in the nervous centres, reflexly in the pons, by volition in the cerebral cortex. The two are intimately connected by connecting elements which decussate in the pontine region, possibly at the corpora quadrigemina. The simple act of head and eyes looking in concert towards an object, is carried on by a diverse system of nerves and muscles which apparently have no anatomical relation one with the other, but all of which, excited by a suitable stimulus, and through the agency of a common centre, act harmoniously together to effect the physiological purpose desired. Any disturbance of this region involves derangement of the conjugate phenomenon as a whole, but leaves the individual elements, with exception of the sixth nerve, to act normally for any other purpose, and in any other form except that of conjugation.

Any portion of the entire conjugate tract from cortex to muscle may be interrupted by disease, and give rise to corresponding symptoms. These, if properly interpreted, enable us, during the life of the patient, to diagnose with considerable accuracy the nature and locality of the lesion.

The clinical facts may be briefly summed up as follows:

1. An irritative lesion of the cortex cerebri (A, Fig. 2),

at the area of conjugate movements, on one side, causes conjugate spasm of the eyeballs and head towards the opposite side, with deviation away from the diseased side of the brain. This is seen in experimental stimulation, and in some cases of epilepsy. Destruction of the same region induces paralysis in the same muscular distribution, with deviation of the eyeballs in a contrary direction, namely towards the diseased hemisphere, owing to the unopposed action of the healthy muscles. This also may be produced experimentally and is met with in severe cases of hæmorrhage or softening accompanying the early stages of hemiplegia. It is in such cases usually a temporary symptom, as the various nervous connections soon enable the other side, by opening out new channels, to perform in this respect the functions of the damaged hemisphere. The same results follow interruption at any portion of the motor tract between A and B, that is, between the cortex and the decussation of fibres in the pons. In such cases also the paralysis of the eyeballs is rarely complete or permanent. They may appear straight at rest, but there is a difficulty in moving them beyond the middle line. The internal rectus however converges readily in association with the other eye, and also by itself when isolated. The affected external rectus can also move the eyeball outwards when the other eye is closed, as the corresponding nucleus and its voluntary connections are unimpaired. Usually in such cases there is no evidence of paresis of the muscles of the neck, and little apparent deviation of the head, for reasons which are obvious, compensation being readily restored through other centres.

2. An irritating lesion, occurring anywhere between B and VI., that is, between the decussation of the motor fibres in the pons, and the sixth nucleus, causes exactly similar symptoms, as No. 1, only the direction of the deviation is reversed, in other words it is towards the side of the lesion. In destructive disease of the same region, the paralysis of the muscles is on the same side as the lesion, and the deviation away from it. The eyeballs can be voluntarily brought to the middle line but no further, and the internal rectus can be made to converge in association with the other

eye, and by itself when alone. The external rectus moves the eyeball outwards when the other eye is closed. The symptoms as in No. 1, are temporary in character, lasting at most for a few days, and the deviation of the head is little if at all observed.

3. Irritation at VI. or at the sixth nucleus itself, causes conjugate deviation of the eyeballs, with rotation and flexion of the head and neck towards the diseased side. Destruction of the same region causes paralysis in a like muscular distribution, with deviation of the eyeballs away from the side of the lesion. In this case the conjugate deformity of the eyeballs is permanent, especially of the eye on the same side as the diseased nucleus, for the nervous connections with the centre which accomplish the conjoint action are broken, and not readily replaced. For the contrary reason the rotation and flexion of the head and neck is only temporary, if seen at all. There is total and permanent palsy of the external rectus of the eye nearest the lesion, with degenerative atrophy of nerve and muscle, the eyeball deviates inwards and cannot be moved outwards as far as the middle line, even when the other eye is closed. The other eye may be brought as far as the middle line, but not beyond it in conjugate association. If, however, both eyes being open, it is brought to converge, or when tested by itself, the other eye being closed, the internal rectus will be found to contract inwards beyond the middle line. This is owing to the fibres which supply the muscle from the sixth nucleus of the opposite side being cut off, and those derived from the third nucleus on the same side being intact. It is obvious that, if a lesion existed in the commissural fibres between the third and the sixth nuclei, accompanied by a second in the motor tract above the latter, that similar results would be produced.

4. A destructive limited lesion immediately in front of the sixth nucleus, involving the fibres of the sixth nerve, causes paralysis of the external rectus of the corresponding eye only, the function of the internal rectus of the other eye remaining intact. There are the usual signs of paralysis of the trunk of the sixth nerve, namely, internal strabismus of the affected eye, and secondary deviation of the other.

The case under notice is an example of No. 3, and this, owing to the preceding considerations, was diagnosed during the life of the patient. That the deviation of the eyeballs was towards the right, and that the lesion was found in the left sixth nucleus, leaves no doubt that the affection of the ocular nerves was a paralytic one. The association between disease of the centre and the conjugate affection is also proved, and if further evidence of lesion of this ganglion is required, it is to be found in the commencing secondary degeneration of the sixth nerve on the affected side. The main difficulty in this case was to account for the *permanent* rotation of the head towards the right side. This could not be owing either to the lesion of the right cortex, or to the destruction of the left sixth nucleus, as in either case such a condition would have been temporary, even if it ever existed at all from such causes. If even under these circumstances weakness of the sterno-mastoid and trapezius and the left flexors of the neck had been produced, the result would have been most fleeting, and soon compensated for by the functionating of the other channels. The most plausible explanation seems to be, that the deformity was caused by active spasm of the left sterno-mastoid muscle, due to direct irritation by the lesion in the sixth nucleus, upon the neighbouring eleventh nucleus, thus causing contraction of the muscle on the same side, through the spinal accessory nerve. Hence the head was tilted over the right shoulder. In favour of this view is the fact that the sterno-mastoid muscle during life was so rigidly contracted that the head could not be brought into the middle line either by voluntary or passive effort, and this condition remained permanent till death.

The facial has very close relations to the sixth nucleus, the fibres of the former coursing round the base of the latter. In this case there was slight paresis of the left side of the face, but this was due to the cortical lesion, and existed prior to the date of the nuclear disease, and moreover the softening was seen to have left the facial fibres intact. There was no evidence of facial rigidity or spasm, which might have occurred from irritation of the seventh nucleus,

but this, even if it existed to a slight extent, may not have been observed, and may have been masked by the other condition of cortical paresis.

The chief subject of regret in this case was the unfortunate loss of the morbid specimens. Happily the nature and exact relations of the lesion were sufficiently observed and figured at the time of the post-mortem examination, as to have served for the foregoing purposes. But opportunities for more delicate investigations, such as the histological characters, and a research into the possible secondary degenerations, for which the parts had been specially reserved, were lost.